Cell and gene therapy in Cambridge, London and Oxford: An invitation to collaborate
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The discovery of the double helix structure of DNA was a great moment in UK science and heralded the dawn of a new era in medicine. The transformation in how we understand and therefore treat disease since then has been staggering. Cell and gene therapies now offer a whole new model and approach for medical science.

Both the discovery of DNA and the more recent Nobel-winning development of induced pluripotent stem cells by Shinya Yamanaka in Kyoto and John Gurdon in Cambridge highlight something that for me is essential for scientific progress – collaboration and team-work. Great discoveries are not made in isolation; they are the product of teams with a variety of expertise, experience and perspectives. Increasingly those teams are international and cross-sector, bringing together the best people from industry and academia around the world.

UK science has a long history of productive collaboration, and the south east region of England in particular is home to some of the best and most exciting research centres and companies in the world, working together to constantly push forward the boundaries of what we know and what we can do.

We are excited at the prospect of what more we can achieve together. MedCity is your guide to the region and is here to help you explore the options.

Paul Nurse
Director
Francis Crick Institute
Section 1 – The opportunity to collaborate

The opportunity to collaborate with the golden triangle: Shared expertise, transformative outcomes

The golden triangle is the world-leading life sciences cluster of Cambridge, London, Oxford and the greater south east region of England. It comprises multiple award-winning research institutions, thousands of talented scientists, deep experience in clinical trials, and a thriving global business and life sciences community. Key to the region’s success has been its collaborative mindset – a drive to embrace and exchange ideas with scientists and professionals from around the world.

Cell and gene therapy are at the heart of the UK government’s long-term strategy for life sciences, and for the translation of great ideas into great partnerships, strong businesses, and, ultimately, ground-breaking therapies.

As such, the golden triangle eagerly invites and welcomes collaborations with colleagues from across the globe in these fields. Many nations share the challenge of improving their populations’ health, and growing or maintaining globally competitive life sciences sectors. The emergence of new, accessible technologies, for instance in gene editing, is driving rapid innovation. Collaboration and exchange are vital to responsibly capture the fruits of that innovation for the benefit of people everywhere. “The golden triangle represents a great place to partner, because of our manufacturing ability and the access we provide to a large ethnically and genetically diverse patient population,” says Eliot Forster, Executive Chair of MedCity and CEO, Immunocore.

There are already countless examples of trans-national collaborations in cell and gene therapy, both in academia and industry. Professors from the UK and Japan in 2012 shared a Nobel Prize in stem cell-related work, opening up entirely new research fields and myriad new opportunities to develop better diagnostic and therapeutic treatments and diagnostics. The UK-China Stem Cell Partnership Initiative is strengthening collaborations with China, while many UK biotech, pharmaceutical firms and academic centres work with counterparts in the US and beyond.

As cell and gene therapy research and development continues to flourish, helped by strong government support and regulatory advances, the golden triangle is calling to researchers, businesses and investors from across the globe. By furthering discovery via shared expertise, developing and refining new techniques while accessing specialist funding and infrastructure, many more revolutionary findings and therapies will emerge, to the benefit of society as a whole.

Eliot Forster
Executive Chair of MedCity and CEO, Immunocore
Cell and gene therapy

Cell and gene therapy, and the technologies associated with and evolving from them, today underpin a large and growing portion of biomedical research.

Cancer immunotherapy, one of the hottest discovery efforts today, encompasses both cell and gene therapy. Chimeric antigen receptor (CAR) T-cell therapy is one approach that genetically reprograms patients’ T-cells, ex vivo, to hunt down and kill cancer cells. These modified T-cells are then infused back into the patient, where they multiply.

Gene therapy – the transfer of genetic materials and the uptake of the gene into the appropriate cells of the body – has come of age to provide marketed treatments for people with rare, inherited genetic diseases.

Techniques such as RNA interference are enjoying a second coming, as targeting and delivery improves, while new gene editing tools such as those based on bacterial CRISPR-associated protein-9 nuclease (Cas 9) may eventually help address a wide range of medical needs. Indeed, “it’s hard to imagine a biotech or pharma company which is not using gene and/or cell therapeutic techniques” in their quest for novel therapeutics, notes Eliot Forster, Executive Chair of MedCity and CEO, Immunocore. “Gene editing, harnessing the pluri-potential activities of cells and stem cell research are all central to a new era of drugs in which modified cells are the engines for therapy. We face a growing population of patients with neuro-degeneration, autoimmune and frailty disorders. I believe cell-based therapies will ultimately be able to solve much of this.”
Section 2 – The ecosystem

The ecosystem

There are many compelling reasons to choose the golden triangle of Cambridge, London, Oxford and the greater south east region of England, for cell and gene therapy partnerships. The region offers an unparalleled ecosystem that includes world-leading science, deep clinical and translational expertise and infrastructure, widespread funding opportunities, a thriving biopharmaceutical business community, and committed government support for life sciences. The Cell Therapy Catapult, based at Guy’s Hospital London, was set up specifically to help translate the best cell therapy and regenerative medicine research into impactful new medicines and methodologies.

Research excellence

As Europe’s leader in cell and gene therapy research and development, the golden triangle already draws scientists, clinicians, entrepreneurs, investors and other professionals from across the globe. The region is home to four of the world’s top ten universities (Imperial College London, University of Cambridge, University of Oxford and University College London) and world-renowned research institutes including the Wellcome Trust, the Wellcome Trust Sanger Institute and the Institute of Cancer Research.

Eliot Forster emphasises that “the UK has a legislative advantage relative to the US when it comes to the manipulation of human cells. There are fewer restrictions and thus a broader ability within the academic and medical community to continue to do cell-based research.”

A clinical trial hotspot

Within its rich ecosystem of universities, hospitals, medical charities, biotechs and pharma, the golden triangle also offers access to a unique clinical trial population via the National Health Service. The NHS has over eight million patients registered in London alone, a highly diverse pool of individuals, and an established point of contact for those seeking to recruit and run trials, in the form of the National Institute for Health Research.

NHS clinicians and nurses, alongside the region’s research institutions, have significant experience running trials; as importantly, they – and their patients – are enthusiastic participants. “Nearly every centre we asked to join a trial said ‘yes’, they wanted to be involved,” says Gregg Sando, CEO of London-based cell therapy firm Cell Medica. “There was great interest in the science, and in wanting to be on the leading edge.”

Professor Bobby Gaspar
Professor of Paediatrics and Immunology, University College London
Translational excellence

The UK has long recognised the need to translate research into marketable therapies, improved health outcomes, successful businesses and a growing economy. The golden triangle has established highly sophisticated technology transfer organisations, and supported investment in world-class production and manufacturing infrastructure. King’s College London’s Cell Therapy Unit is Europe’s largest GMP lab facility for cellular and gene therapies used in trials and academia. In 2017 the Cell Therapy Catapult will open a major £55 million manufacturing centre on the Stevenage BioScience Catalyst campus, north of London; this will be used to make late phase clinical trial and commercial supply of cell and gene therapies.

London is also home to the UK drugs regulator, the Medicines and Healthcare products Regulatory Agency (MHRA), plus the world-class healthcare assessment agency, the National Institute of Health and Clinical Excellence (NICE).

The National Institute for Health and Care Excellence (NICE)

The National Institute for Health and Care Excellence (NICE) technology appraisal programme reviews clinical and economic evidence to set recommendations on the use of new and existing medicines for the NHS in England. The evaluation and decision making frameworks for the programme compare the clinical and cost effectiveness of a diverse range of medicines for different disease areas. These methods can also be applied to regenerative medicines and cell therapies. The UK Regenerative Medicine Expert Group, which NICE was actively involved in, identified areas where evaluating regenerative medicine and cell therapies was particularly complex and recommended that NICE investigate these complexities and propose potential solutions. This study is in progress and includes consideration of a hypothetical CAR-T cell product for treating acute lymphoblastic leukaemia, with characteristics based on early clinical data for related treatments supplemented with hypothetical evidence. It explores multiple scenarios, varying parameters such as estimates of effectiveness, maturity of evidence, discounting rates applied, price and payment models and managed access arrangements.
Section 2 – The ecosystem

Diverse biopharma talent

The region’s strong scientific and clinical base, coupled with London’s status as a global financial centre, has helped generate Europe’s leading cluster of cell and gene therapy start-ups. These include T-cell-focused Adaptimmune, Oxford-based Immunocore, which recently secured the biggest ever private fundraising by a European biotech, Cell Medica in London, and newly-founded Autolus, which is working on engineered chimeric antigen receptors (CAR) T-cell products. Meanwhile, established players such as gene therapy-focused Oxford BioMedica, listed on the London Stock Exchange, and AIM-listed ReNeuron PLC, continue to lead in their respective fields.

The region also draws in large multinational pharmaceutical and biotech firms hungry for talent, new science, and partnerships. Pfizer set up its gene therapy unit in London in late 2014; about the same time that Japan’s Tokyo Electron Limited chose the Stevenage Bioscience Catalyst to launch its open innovation stem cell technology centre, to develop smart cell processing technologies. AstraZeneca recently chose Cambridge for its new global R&D hub, joining other multinational R&D players in the area, including Takeda. US-headquartered Gilead Sciences in February 2015 announced it too was expanding its R&D in Cambridge, as well as opening a new UK commercial headquarters in London.

Fantastic funding opportunities

These strategic investors, plus the City of London’s growing venture capital and institutional investment communities, and world-class research institutions, provide research partners and entrepreneurs with an expanding suite of funding opportunities.

“The UK gets a really big tick for funding options,” enthuses Cell Medica’s CEO, Gregg Sando. Besides the Medical Research Council and Innovate UK, a public body which supports science and technology innovations, he singles out the Wellcome Trust as “a tremendous force” for helping to translate academic ideas into commercial products in the biomedical sector.

Further downstream, almost $2 billion was raised in life sciences IPOs and follow-on offerings on the London Stock Exchange in 2014.
Committed, focused government support

The UK benefits from sustained long-term commitment to life sciences. In 2014 it became the first country to appoint a dedicated Minister for Life Sciences: industry veteran George Freeman. His work includes fast-tracking the uptake of new drugs and technologies with a particular focus on genomics and regenerative medicine.

Government-funded organisations such as Innovate UK are dedicated to building successful businesses, while newer more focused initiatives such as the Cell Therapy Catapult have also emerged, specifically to encourage and de-risk gene therapy and regenerative medicine.

The UK’s suite of support for business and innovation includes Patent Box, which reduces corporation tax on profits resulting from patented inventions, and R&D tax credits, tax relief for small and mid-sized enterprises that engage in R&D, making the UK an extremely competitive place to invest and invent.

Bringing these strengths together is MedCity, launched by Mayor of London Boris Johnson in April 2014. MedCity is a unique portal for the international life sciences industry to access and collaborate with the region’s expertise.

George Freeman MP
Parliamentary Under Secretary of State for Life Sciences
Rich networks, deep talent, ideal time-zone

By providing access to rich networks of expertise and financial support, these programmes draw on and further encourage Cambridge, London and Oxford’s collaborative, cross-disciplinary culture of open innovation. The golden triangle already benefits from the UK’s lower-than-average corporation tax rates; the region is also ideally located geographically between the major time-zones of the US and Far East.

Add to that the compelling need for most of the world’s best scientists to learn English, and it’s easy to see why the region assembles an ‘incredible pool of scientific and medical people,’ according to Cell Medica CEO, Gregg Sando. In London alone, for example, there are 40 universities with around 96,800 students and 29,600 graduates in life sciences1.

Therefore, the golden triangle offers unmissable opportunities for its scientific and business communities, as well as for their actual and future partners.

The golden triangle’s office hours overlap with those countries that collectively account for 99% of the world’s GDP.

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1: HESA, 2013/14
2: OAG
A snapshot of what is happening in specialist cell therapy institutes across the region

The Cell Therapy Catapult

The Cell Therapy Catapult, based at Guy’s Hospital in London, is an innovation centre translating cell and gene therapy research projects into life-saving medicines. Set up in 2012 to support cell therapy businesses, the Cell Therapy Catapult provides clinical trial, technical, manufacturing, regulatory and market access expertise.

The Cell Therapy Catapult also develops key UK infrastructure capabilities and technological innovations, such as the cell therapy manufacturing centre in Stevenage. This secure, compliant 7200m² facility will allow developers from across the world to reliably ship UK-manufactured cell-lines and cell-based products into the European Union within 24 hours.

In addition, under an agreement with iPS Academia Japan, the Cell Therapy Catapult is permitted to sub-license, manufacture and commercialise iPS cell lines for use in early-stage research and clinical trials. This enables the UK to be a centre for iPS technologies and potentially cuts development times by up to two years.

Partners such as leading US company Athersys Limited and Japan based Tokyo Electron rely on the Cell Therapy Catapult for their experience and expertise. The Cell Therapy Catapult is currently working with Athersys Limited to support a Phase I/II clinical study evaluating the administration of MultiStem® therapy to Acute Respiratory Distress Syndrome patients. The study will be conducted in conjunction with the Cell Therapy Catapult and leading clinical sites across the UK.

For Bob Honda, Director of STC and Tokyo Electron Europe Limited (TEE), the Cell Therapy Catapult’s support has been central: “Tokyo Electron chose to locate its Stem Cell Technology Centre (STC) in the UK because of the industry support the Cell Therapy Catapult provides, and the world-leading scientific research conducted in the country.”
“Thanks to the Cell Therapy Catapult, the Wellcome Trust and other public bodies, as an entrepreneur in London, you feel the wind is behind you.”

Gregg Sando, CEO Cell Medica
Oxford: Collaborating to uncover stem cell opportunities

Oxford, just one of the clusters of scientific excellence within the golden triangle, boasts a dynamic network of stem cell focused researchers, institutes and innovation.

The Oxford Stem Cell Institute brings together over 40 laboratories across the city with a shared ambition to promote stem cell therapies for patient benefit, using their combined scientific and clinical expertise. The institute recognises the need for cross-disciplinary research – overcoming taxonomic barriers between cancer, regenerative medicine and traditional drug development.

Oxford is also the lead academic institution within the five year StemBANCC research programme, a €55.6 million European project funded by the Innovative Medicines Initiative. StemBANCC assembles partners from 11 countries, and aims to generate human-induced pluripotent stem cells (iPSC) as a platform for drug discovery, in particular in brain diseases and diabetes. The project is riding on the wave of international iPSC research, driven from Shinya Yamanaka’s work.

Reflecting the translational excellence across the region, a new company, OxStem, has been set up to spin out cell therapy focused companies from the University of Oxford. OxStem will leverage both stem cell and medicinal chemistry expertise within the University and other partners to create and spin-out a series of daughter companies focused on different therapy areas, such as dementia or macular degeneration in the eye. These ‘Stem’ companies will ultimately deliver small molecule therapeutics that work by activating repair mechanisms already present within the body, rather than manipulating cells in vitro before re-insertion. Acting as a parent holding company, OxStem funds the spin offs, as well as licensing its IP.
Cambridge: Novel, cross-disciplinary approaches to treat osteoarthritis

Scientists at the University of Cambridge Stem Cell Institute, funded by the Wellcome Trust/Medical Research Council, are ideally placed to collaborate and network with neighbouring disciplines, research institutes and industry, both within Cambridge’s rich biomedical talent pool and beyond. They are exploring stem cells’ fundamental properties, function and their role in disease, as well as seeking to harness endogenous stem and progenitor cells for repair and regeneration.

The Institute works with affiliate scientists whose research intersects with stem cell biology and medicine. One of these is Andrew McCaskie, Professor of Orthopedic Surgery at the University of Cambridge. McCaskie and Cambridge Stem Cell Institute Director, Professor Austin Smith, are investigating whether stem cells and related regenerative techniques could allow damaged joints in patients with osteoarthritis to be repaired, thereby radically changing the way the condition is treated.

‘The conventional approach is to treat osteoarthritis when the joint is extensively damaged by using a joint replacement. We want to treat the condition at an earlier stage, using repair and regenerative techniques to prolong the use of the patient’s own joint and therefore defer joint replacement,’ says McCaskie.

McCaskie leads two other multicentre, collaborative efforts – each with a strong focus on translating great science into great products. The Arthritis Research UK Tissue Engineering Centre, assembling universities and hospitals across the UK, focuses on both cell and cell-free approaches to regenerative therapies in osteoarthritis. The SmartStep consortium (“Stepwise Translational Pathway for Smart Material Cell Therapy”), funded via the UK Regenerative Medicine Platform, an initiative that is addressing the key translational challenges of regenerative medicine, is exploring ways to stimulate the patient’s own repair mechanisms by targeting different cell populations. This will have a particular focus on novel biomaterials and bioactive molecules that may help recruit and differentiate resident stem and/or progenitor cells within the joints. SmartStep includes investigators from across the UK and the Netherlands.
Cell therapy in action

Pfizer and the Global Medical Excellence Cluster (GMEC)

Pfizer has over 20 years’ experience in rare diseases and is dedicated to discovering more new medicines. They have two operations in London supporting this goal.

Both work on the principles of collaboration. Pfizer believes that no one person has all the answers – by working together, they can achieve more and faster.

The Genetic Medicine Institute is a new research facility dedicated to the development of genetic medicines at pace and scale. They are exploring how to use viruses as tools to replace or repair faulty genes. Located in the heart of London’s science community, the Genetic Medicine Institute supports the free flow of knowledge, ideas and best practice between industry and academia.

Pfizer has also joined with fifteen of the UK’s leading universities to create the Rare Disease Consortium (RDC). Initially a partnership between Pfizer and the Global Medical Excellence Cluster (GMEC), which includes University of Cambridge, Imperial College London, King’s College London, University of Oxford, University College London and Queen Mary University of London, the consortium has expanded to include the N8 research group in north England as well as the University of Dundee.

The RDC has recently initiated research into read-through disorders with the University of Dundee, in haematology and neuromuscular disorders with the University of Oxford and neuromuscular disorders with Oxford, Imperial College London and University College London.

In a recent government report, Pfizer was recognised as the most active collaborator in UK university research, headquartered outside the UK.
Section 3 – Cell therapy in action

Imperial College London: Healing broken hearts

A multi-disciplinary group at Imperial College London is bringing together bioengineers, material scientists, chemists, surgeons and biologists to create biomaterials that enable the body to regenerate.

Led by Molly Stevens, Professor of Biomedical Materials and Regenerative Medicine, the group is developing novel ways to regenerate bones, cartilage and heart cells. Their pioneering work includes the development of implantable biomaterials that can coax the body into repairing damaged tissue. These biomaterials come in varied forms such as gels for minimally invasive delivery and also 3D foam scaffolds.

The team is focused on using regenerative techniques to help fix bone tissue and heart tissue for a range of applications, from arrhythmia to heart attack recovery. Recent work includes the demonstration that cardiac stem cells can switch to become heart muscle cells when stimulated with micropatterned biomaterials. According to Professor Stevens, the ability to generate biomaterials to help in orthopaedic and heart regeneration has huge potential to save and improve the lives of people affected by heart disease and orthopaedic traumas, which are a major source of disability worldwide. She says:

“We are getting much better at treating heart disease but the damage to the heart after a heart attack can make people more vulnerable to heart failure and impede their quality of life. We are developing biomaterials that provide a better match to healthy heart tissue to encourage its regeneration.”

Application of the group’s research is an important priority for Professor Stevens, who is passionate about the potential of regenerative medicine to save and improve lives. She is working with many academic groups around the world including at UCLA and MIT, as well as a number of industrial partners from SMEs to large pharma. She previously established the spin-out company RepRegen, to develop smart biomaterials for bone and wound repair. Her group’s research has been recognised by over 20 major international awards including the EU40 Award for the best materials scientist in Europe under 40.
Earlier in 2015, Japan’s largest pharmaceutical company Takeda joined forces with University College London to find new targets to treat a range of neurodegenerative diseases including Huntington’s, Parkinson’s and Motor Neuron diseases. The partners will use established cell lines from both patients and their healthy relatives to better understand the mechanisms of various CNS disorders, and to discover improved treatments.

The collaboration was driven from Takeda’s Cambridge-based UK research hub, and made possible by the Japanese group’s established presence in the golden triangle, including clinical development offices in London. “Cambridge is only a 50 minute train ride from London,” remarks Mark Carlton, President of Takeda Cambridge. “When University College London collaborators come up here, they often have ex-PhD students and other colleagues that they can also meet with.” Takeda Cambridge has doubled its headcount to around 150 highly skilled scientists, thanks to the rich pool of talent, willing to work in an area with many employment opportunities across biotech, academia and pharmaceuticals.

Takeda selected University College London after scrutinising a range of potential partners. What set the London-based group apart was the level and depth of coordination and professionalism within their neurology group, Mark Carlton recalls, as well as the quality of their research proposals. Technologies and data banks were another big plus: “When they collect patient tissue, they also collect from healthy relatives, so you can compare genetically closely-aligned cell types. That offers a powerful control reducing the ‘noise’ in the dataset,” says Mark Carlton.

Carlton is excited about the promise of CNS research in the era of Big Data and genomics in particular. “We’re at a turning point in CNS research,” he says, describing the beginnings of patient and disease stratification. Joint government and industry-funded initiatives such as Genomics England, whose aim is to sequence 100,000 genomes of people with conditions including cancer, CNS disorders and rare diseases, will provide valuable data to allow an improved understanding of causal events driving these conditions. “We’ll see important changes in the coming years, in imaging, patient stratification, and in clinical trial design,” he predicts.

Takeda’s interest in cell and gene therapy research extends well beyond CNS; the group has also been working since 2014 with University College London on using induced pluripotent stem cells to treat muscular dystrophy. This partnership, run out of Takeda’s US-based New Frontiers group, is also looking at novel cell and gene therapy strategies using artificial human chromosomes and novel biomaterials.

“When they collect patient tissue, they also collect from healthy relatives, so you can compare genetically closely-aligned cell types. That offers a powerful control!”

Dr Mark Carlton  
President and Chief Scientific Officer, Takeda
Cell Medica: Showcasing UK science, trials, funding and support

Cell Medica's evolution illustrates the UK's dynamic research and clinical trial environment, its commercial focus, and its extensive funding and support networks.

The London-based company was set up in 2007 around an adoptive T-cell immunotherapy project that was already undergoing early trials in an academic setting. The start-up's goal was to take the programme to the next level – into market-focused, confirmatory trials. Adoptive T-cell immunotherapy involves transferring a virus-specific T-cell from a healthy donor, to restore immunity to that virus in a bone marrow transplant patient, for example a patient with leukemia or another haematological malignancy.

Researchers at University College London, the Royal Free Hospital and the University of Birmingham had been pioneering this new paradigm for treating patients so “the UK was a natural place to set up the company,” explains CEO Gregg Sando. Their product, Cytovir CMV, for the prevention of infections in bone marrow transplant patients, has since been the subject of two randomised clinical trials across 15 UK transplant centres, part-funded by the Wellcome Trust. “We had a good experience of running clinical trials in the UK” concludes Gregg Sando. “Nearly every centre that we asked to join a trial said yes, because it was interesting science, and they wanted to be involved.”

Cell Medica has also benefited from financial support from Innovate UK, which provided £2 million for the company to develop, in partnership with University College London, a more cost-effective system for manufacturing T-cell products as well as funding development and testing of a new product targeting adenovirus infection in children receiving transplants. It is also working with the Cell Therapy Catapult to achieve NHS reimbursement for Cytovir CMV.

In November 2014, Cell Medica raised £50 million in a Series B that included three of the UK’s most significant life sciences investors: Imperial Innovations, Invesco Perpetual and Woodford Investment Management.

Imperial Innovations engages in technology transfer, licensing, company incubation and investment, with a focus on IP generated at or associated with four top institutions in the UK's golden triangle: Imperial College London, Universities of Oxford and Cambridge, and University College London. The group has invested over £1 billion in UK innovation.
What next?

With a world-leading scientific pedigree, a history of effective partnerships in life sciences and flourishing research and development in cell and gene therapy, the golden triangle is very open to collaborating with organisations and companies from across the globe.

If you would like the opportunity to work with organisations and institutions within the golden triangle, both MedCity and London & Partners can help you access this thriving life sciences region.

MedCity can help you navigate and access different parts of the academic, NHS and industrial life sciences and healthcare environment across the golden triangle of Cambridge, London, Oxford and the greater south east region of England.

London & Partners is the official promotional company for London and the experts on doing business in the capital, helping overseas businesses to set up, and grow. The team can advise, free of charge, on every aspect of locating and doing business in the city.

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“World-class research and publications, great clinical centres, talent, strong government support, industry-academic collaborations, regulatory expertise – all this has made the golden triangle a major melting pot for cell and gene therapy.”

Professor Chris Mason, Chair of Regenerative Medicine Bioprocessing at University College London
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